

SUBSTITUTE
SEQUENCE LISTING

5 (1) GENERAL INFORMATION:

(i) APPLICANT: TOCQUE, Bruno
WASYLYK, Bohdan
DUBS-POTERSZMAN,
Marie-Christine

(ii) TITLE OF INVENTION: ANTAGONISTS OF THE ONCOGENIC ACTIVITY OF
THE PROTEIN MDM2, AND USE THEREOF IN THE TREATMENT OF
CANCERS

(iii) NUMBER OF SEQUENCES: 4

(iv) CORRESPONDENCE ADDRESS:

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(C) CITY: Collegeville
(D) STATE: PA
(E) COUNTRY: USA
(F) ZIP: 19426

(v) COMPUTER READABLE FORM:

(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.30

(vi) CURRENT APPLICATION DATA:

(A) APPLICATION NUMBER:
(B) FILING DATE:
(C) CLASSIFICATION:

(vii) PRIOR APPLICATION DATA:

(A) APPLICATION NUMBER: FR 96/01340
(B) FILING DATE: 02-SEP-1996

(vii) PRIOR APPLICATION DATA:

(A) APPLICATION NUMBER: WO FR95/10331
(B) FILING DATE: 04-SEP-1995

(viii) ATTORNEY/AGENT INFORMATION:

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(C) REFERENCE/DOCKET NUMBER: ST95050-US

(ix) TELECOMMUNICATION INFORMATION:

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55 (2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1476 base pairs

(B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: other nucleic acid
 (A) DESCRIPTION: /desc = "Oligonucleotide"

10 (ix) FEATURE:
 (A) NAME/KEY: CDS
 (B) LOCATION: 1..1473

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

15	ATG TGC AAT ACC AAC ATG TCT GTA CCT ACT GAT GGT GCT GTA ACC ACC	48
	Met Cys Asn Thr Asn Met Ser Val Pro Thr Asp Gly Ala Val Thr Thr	
	1 5 10 15	
20	TCA CAG ATT CCA GCT TCG GAA CAA GAG ACC CTG GTT AGA CCA AAG CCA	96
	Ser Gln Ile Pro Ala Ser Glu Gln Glu Thr Leu Val Arg Pro Lys Pro	
	20 25 30	
25	TTG CTT TTG AAG TTA TTA AAG TCT GTT GGT GCA CAA AAA GAC ACT TAT	144
	Leu Leu Leu Lys Leu Leu Lys Ser Val Gly Ala Gln Lys Asp Thr Tyr	
	35 40 45	
30	ACT ATG AAA GAG GTT CTT TTT TAT CTT GGC CAG TAT ATT ATG ACT AAA	192
	Thr Met Lys Glu Val Leu Phe Tyr Leu Gly Gln Tyr Ile Met Thr Lys	
	50 55 60	
35	CGA TTA TAT GAT GAG AAG CAA CAA CAT ATT GTA TAT TGT TCA AAT GAT	240
	Arg Leu Tyr Asp Glu Lys Gln Gln His Ile Val Tyr Cys Ser Asn Asp	
	65 70 75 80	
40	CTT CTA GGA GAT TTG TTT GGC GTG CCA AGC TTC TCT GTG AAA GAG CAC	288
	Leu Leu Gly Asp Leu Phe Gly Val Pro Ser Phe Ser Val Lys Glu His	
	85 90 95	
45	AGG AAA ATA TAT ACC ATG ATC TAC AGG AAC TTG GTA GTA GTC AAT CAG	336
	Arg Lys Ile Tyr Thr Met Ile Tyr Arg Asn Leu Val Val Val Asn Gln	
	100 105 110	
50	CAG GAA TCA TCG GAC TCA GGT ACA TCT GTG AGT GAG AAC AGG TGT CAC	384
	Gln Glu Ser Ser Asp Ser Gly Thr Ser Val Ser Glu Asn Arg Cys His	
	115 120 125	
55	CTT GAA GGT GGG AGT GAT CAA AAG GAC CTT GTA CAA GAG CTT CAG GAA	432
	Leu Glu Gly Gly Ser Asp Gln Lys Asp Leu Val Gln Glu Leu Gln Glu	
	130 135 140	
60	GAG AAA CCT TCA TCT TCA CAT TTG GTT TCT AGA CCA TCT ACC TCA TCT	480
	Glu Lys Pro Ser Ser Ser His Leu Val Ser Arg Pro Ser Thr Ser Ser	
	145 150 155 160	
65	AGA AGG AGA GCA ATT AGT GAG ACA GAA GAA AAT TCA GAT GAA TTA TCT	528
	Arg Arg Arg Ala Ile Ser Glu Thr Glu Glu Asn Ser Asp Glu Leu Ser	
	165 170 175	

	GGT GAA CGA CAA AGA AAA CGC CAC AAA TCT GAT AGT ATT TCC CTT TCC	576
	Gly Glu Arg Gln Arg Lys Arg His Lys Ser Asp Ser Ile Ser Leu Ser	
	180 185 190	
5	TTT GAT GAA AGC CTG GCT CTG TGT GTA ATA AGG GAG ATA TGT TGT GAA	624
	Phe Asp Glu Ser Leu Ala Leu Cys Val Ile Arg Glu Ile Cys Cys Glu	
	195 200 205	
10	AGA AGC AGT AGC AGT GAA TCT ACA GGG ACG CCA TCG AAT CCG GAT CTT	672
	Arg Ser Ser Ser Ser Glu Ser Thr Gly Thr Pro Ser Asn Pro Asp Leu	
	210 215 220	
15	GAT GCT GGT GTA AGT GAA CAT TCA GGT GAT TGG TTG GAT CAG GAT TCA	720
	Asp Ala Gly Val Ser Glu His Ser Gly Asp Trp Leu Asp Gln Asp Ser	
	225 230 235 240	
20	GTT TCA GAT CAG TTT AGT GTA GAA TTT GAA GTT GAA TCT CTC GAC TCA	768
	Val Ser Asp Gln Phe Ser Val Glu Phe Glu Val Glu Ser Leu Asp Ser	
	245 250 255	
	GAA GAT TAT AGC CTT AGT GAA GAA GGA CAA GAA CTC TCA GAT GAA GAT	816
	Glu Asp Tyr Ser Leu Ser Glu Glu Gly Gln Glu Leu Ser Asp Glu Asp	
	260 265 270	
25	GAT GAG GTA TAT CAA GTT ACT GTG TAT CAG GCA GGG GAG AGT GAT ACA	864
	Asp Glu Val Tyr Gln Val Thr Val Tyr Gln Ala Gly Glu Ser Asp Thr	
	275 280 285	
30	GAT TCA TTT GAA GAA GAT CCT GAA ATT TCC TTA GCT GAC TAT TGG AAA	912
	Asp Ser Phe Glu Glu Asp Pro Glu Ile Ser Leu Ala Asp Tyr Trp Lys	
	290 295 300	
35	TGC ACT TCA TGC AAT GAA ATG AAT CCC CCC CTT CCA TCA CAT TGC AAC	960
	Cys Thr Ser Cys Asn Glu Met Asn Pro Pro Leu Pro Ser His Cys Asn	
	305 310 315 320	
40	AGA TGT TGG GCC CTT CGT GAG AAT TGG CTT CCT GAA GAT AAA GGG AAA	1008
	Arg Cys Trp Ala Leu Arg Glu Asn Trp Leu Pro Glu Asp Lys Gly Lys	
	325 330 335	
	GAT AAA GGG GAA ATC TCT GAG AAA GCC AAA CTG GAA AAC TCA ACA CAA	1056
	Asp Lys Gly Glu Ile Ser Glu Lys Ala Lys Leu Glu Asn Ser Thr Gln	
	340 345 350	
45	GCT GAA GAG GGC TTT GAT GTT CCT GAT TGT AAA AAA ACT ATA GTG AAT	1104
	Ala Glu Glu Gly Phe Asp Val Pro Asp Cys Lys Lys Thr Ile Val Asn	
	355 360 365	
50	GAT TCC AGA GAG TCA TGT GTT GAG GAA AAT GAT GAT AAA ATT ACA CAA	1152
	Asp Ser Arg Glu Ser Cys Val Glu Glu Asn Asp Asp Lys Ile Thr Gln	
	370 375 380	
55	GCT TCA CAA TCA CAA GAA AGT GAA GAC TAT TCT CAG CCA TCA ACT TCT	1200
	Ala Ser Gln Ser Gln Glu Ser Glu Asp Tyr Ser Gln Pro Ser Thr Ser	
	385 390 395 400	
	AGT AGC ATT ATT TAT AGC AGC CAA GAA GAT GTG AAA GAG TTT GAA AGG	1248

Ser Ser Ile Ile Tyr Ser Ser Gln Glu Asp Val Lys Glu Phe Glu Arg
405 410 415

5 GAA GAA ACC CAA GAC AAA GAA GAG AGT GTG GAA TCT AGT TTG CCC CTT 1296
Glu Glu Thr Gln Asp Lys Glu Glu Ser Val Glu Ser Ser Leu Pro Leu
420 425 430

10 AAT GCC ATT GAA CCT TGT GTG ATT TGT CAA GGT CGA CCT AAA AAT GGT 1344
Asn Ala Ile Glu Pro Cys Val Ile Cys Gln Gly Arg Pro Lys Asn Gly
435 440 445

15 TGC ATT GTC CAT GGC AAA ACA GGA CAT CTT ATG GCC TGC TTT ACA TGT 1392
Cys Ile Val His Gly Lys Thr Gly His Leu Met Ala Cys Phe Thr Cys
450 455 460

GCA AAG AAG CTA AAG AAA AGG AAT AAG CCC TGC CCA GTA TGT AGA CAA 1440
Ala Lys Lys Leu Lys Lys Arg Asn Lys Pro Cys Pro Val Cys Arg Gln
465 470 475 480

20 CCA ATT CAA ATG ATT GTG CTA ACT TAT TTC CCC TAG 1476
Pro Ile Gln Met Ile Val Leu Thr Tyr Phe Pro
485 490

25 (2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 491 amino acids
(B) TYPE: amino acid
30 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

35 Met Cys Asn Thr Asn Met Ser Val Pro Thr Asp Gly Ala Val Thr Thr
1 5 10 15

40 Ser Gln Ile Pro Ala Ser Glu Gln Glu Thr Leu Val Arg Pro Lys Pro
20 25 30

Leu Leu Leu Lys Leu Leu Lys Ser Val Gly Ala Gln Lys Asp Thr Tyr
35 40 45

45 Thr Met Lys Glu Val Leu Phe Tyr Leu Gly Gln Tyr Ile Met Thr Lys
50 55 60

Arg Leu Tyr Asp Glu Lys Gln Gln His Ile Val Tyr Cys Ser Asn Asp
65 70 75 80

50 Leu Leu Gly Asp Leu Phe Gly Val Pro Ser Phe Ser Val Lys Glu His
85 90 95

Arg Lys Ile Tyr Thr Met Ile Tyr Arg Asn Leu Val Val Val Asn Gln
55 100 105 110

Gln Glu Ser Ser Asp Ser Gly Thr Ser Val Ser Glu Asn Arg Cys His
115 120 125

	Leu	Glu	Gly	Gly	Ser	Asp	Gln	Lys	Asp	Leu	Val	Gln	Glu	Leu	Gln	Glu	
	130						135					140					
5	Glu	Lys	Pro	Ser	Ser	Ser	His	Leu	Val	Ser	Arg	Pro	Ser	Thr	Ser	Ser	
	145					150					155					160	
	Arg	Arg	Arg	Ala	Ile	Ser	Glu	Thr	Glu	Glu	Asn	Ser	Asp	Glu	Leu	Ser	
					165					170					175		
10	Gly	Glu	Arg	Gln	Arg	Lys	Arg	His	Lys	Ser	Asp	Ser	Ile	Ser	Leu	Ser	
				180					185					190			
	Phe	Asp	Glu	Ser	Leu	Ala	Leu	Cys	Val	Ile	Arg	Glu	Ile	Cys	Cys	Glu	
15			195					200					205				
	Arg	Ser	Ser	Ser	Ser	Glu	Ser	Thr	Gly	Thr	Pro	Ser	Asn	Pro	Asp	Leu	
		210					215					220					
20	Asp	Ala	Gly	Val	Ser	Glu	His	Ser	Gly	Asp	Trp	Leu	Asp	Gln	Asp	Ser	
	225					230					235					240	
	Val	Ser	Asp	Gln	Phe	Ser	Val	Glu	Phe	Glu	Val	Glu	Ser	Leu	Asp	Ser	
					245					250					255		
25	Glu	Asp	Tyr	Ser	Leu	Ser	Glu	Glu	Gly	Gln	Glu	Leu	Ser	Asp	Glu	Asp	
				260					265					270			
	Asp	Glu	Val	Tyr	Gln	Val	Thr	Val	Tyr	Gln	Ala	Gly	Glu	Ser	Asp	Thr	
30			275					280					285				
	Asp	Ser	Phe	Glu	Glu	Asp	Pro	Glu	Ile	Ser	Leu	Ala	Asp	Tyr	Trp	Lys	
		290					295					300					
35	Cys	Thr	Ser	Cys	Asn	Glu	Met	Asn	Pro	Pro	Leu	Pro	Ser	His	Cys	Asn	
	305					310					315					320	
	Arg	Cys	Trp	Ala	Leu	Arg	Glu	Asn	Trp	Leu	Pro	Glu	Asp	Lys	Gly	Lys	
					325					330					335		
40	Asp	Lys	Gly	Glu	Ile	Ser	Glu	Lys	Ala	Lys	Leu	Glu	Asn	Ser	Thr	Gln	
				340					345					350			
	Ala	Glu	Glu	Gly	Phe	Asp	Val	Pro	Asp	Cys	Lys	Lys	Thr	Ile	Val	Asn	
45			355					360					365				
	Asp	Ser	Arg	Glu	Ser	Cys	Val	Glu	Glu	Asn	Asp	Asp	Lys	Ile	Thr	Gln	
		370					375					380					
50	Ala	Ser	Gln	Ser	Gln	Glu	Ser	Glu	Asp	Tyr	Ser	Gln	Pro	Ser	Thr	Ser	
	385					390					395					400	
	Ser	Ser	Ile	Ile	Tyr	Ser	Ser	Gln	Glu	Asp	Val	Lys	Glu	Phe	Glu	Arg	
					405					410					415		
55	Glu	Glu	Thr	Gln	Asp	Lys	Glu	Glu	Ser	Val	Glu	Ser	Ser	Leu	Pro	Leu	
				420					425					430			

Asn Ala Ile Glu Pro Cys Val Ile Cys Gln Gly Arg Pro Lys Asn Gly
 435 440 445

Cys Ile Val His Gly Lys Thr Gly His Leu Met Ala Cys Phe Thr Cys
 5 450 455 460

Ala Lys Lys Leu Lys Lys Arg Asn Lys Pro Cys Pro Val Cys Arg Gln
 465 470 475 480

10 Pro Ile Gln Met Ile Val Leu Thr Tyr Phe Pro
 485 490

(2) INFORMATION FOR SEQ ID NO:3:

15 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 1182 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: other nucleic acid
 (A) DESCRIPTION: /desc = "Oligonucleotide"

25 (ix) FEATURE:
 (A) NAME/KEY: CDS
 (B) LOCATION: 1..1179

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

	ATG GAG GAG CCG CAG TCA GAT CCT AGC GTC GAG CCC CCT CTG AGT CAG	48
	Met Glu Glu Pro Gln Ser Asp Pro Ser Val Glu Pro Pro Leu Ser Gln	
	495 500 505	
35	GAA ACA TTT TCA GAC CTA TGG AAA CTA CTT CCT GAA AAC AAC GTT CTG	96
	Glu Thr Phe Ser Asp Leu Trp Lys Leu Leu Pro Glu Asn Asn Val Leu	
	510 515 520	
40	TCC CCC TTG CCG TCC CAA GCA ATG GAT GAT TTG ATG CTG TCC CCG GAC	144
	Ser Pro Leu Pro Ser Gln Ala Met Asp Asp Leu Met Leu Ser Pro Asp	
	525 530 535	
45	GAT ATT GAA CAA TGG TTC ACT GAA GAC CCA GGT CCA GAT GAA GCT CCC	192
	Asp Ile Glu Gln Trp Phe Thr Glu Asp Pro Gly Pro Asp Glu Ala Pro	
	540 545 550 555	
50	AGA ATG CCA GAG GCT GCT CCC CCC GTG GCC CCT GCA CCA GCA GCT CCT	240
	Arg Met Pro Glu Ala Ala Pro Pro Val Ala Pro Ala Pro Ala Ala Pro	
	560 565 570	
55	ACA CCG GCG GCC CCT GCA CCA GCC CCC TCC TGG CCC CTG TCA TCT TCT	288
	Thr Pro Ala Ala Pro Ala Pro Ala Pro Ser Trp Pro Leu Ser Ser Ser	
	575 580 585	
	GTC CCT TCC CAG AAA ACC TAC CAG GGC AGC TAC GGT TTC CGT CTG GGC	336
	Val Pro Ser Gln Lys Thr Tyr Gln Gly Ser Tyr Gly Phe Arg Leu Gly	
	590 595 600	

	TTC	TTG	CAT	TCT	GGG	ACA	GCC	AAG	TCT	GTG	ACT	TGC	ACG	TAC	TCC	CCT	384
	Phe	Leu	His	Ser	Gly	Thr	Ala	Lys	Ser	Val	Thr	Cys	Thr	Tyr	Ser	Pro	
	605						610					615					
5	GCC	CTC	AAC	AAG	ATG	TTT	TGC	CAA	CTG	GCC	AAG	ACC	TGC	CCT	GTG	CAG	432
	Ala	Leu	Asn	Lys	Met	Phe	Cys	Gln	Leu	Ala	Lys	Thr	Cys	Pro	Val	Gln	
	620					625					630					635	
10	CTG	TGG	GTT	GAT	TCC	ACA	CCC	CCG	CCC	GGC	ACC	CGC	GTC	CGC	GCC	ATG	480
	Leu	Trp	Val	Asp	Ser	Thr	Pro	Pro	Pro	Gly	Thr	Arg	Val	Arg	Ala	Met	
					640					645					650		
15	GCC	ATC	TAC	AAG	CAG	TCA	CAG	CAC	ATG	ACG	GAG	GTT	GTG	AGG	CGC	TGC	528
	Ala	Ile	Tyr	Lys	Gln	Ser	Gln	His	Met	Thr	Glu	Val	Val	Arg	Arg	Cys	
				655					660					665			
20	CCC	CAC	CAT	GAG	CGC	TGC	TCA	GAT	AGC	GAT	GGT	CTG	GCC	CCT	CCT	CAG	576
	Pro	His	His	Glu	Arg	Cys	Ser	Asp	Ser	Asp	Gly	Leu	Ala	Pro	Pro	Gln	
			670					675					680				
25	CAT	CTT	ATC	CGA	GTG	GAA	GGA	AAT	TTG	CGT	GTG	GAG	TAT	TTG	GAT	GAC	624
	His	Leu	Ile	Arg	Val	Glu	Gly	Asn	Leu	Arg	Val	Glu	Tyr	Leu	Asp	Asp	
		685					690					695					
30	AGA	AAC	ACT	TTT	CGA	CAT	AGT	GTG	GTG	GTG	CCC	TAT	GAG	CCG	CCT	GAG	672
	Arg	Asn	Thr	Phe	Arg	His	Ser	Val	Val	Val	Pro	Tyr	Glu	Pro	Pro	Glu	
	700					705					710					715	
35	GTT	GGC	TCT	GAC	TGT	ACC	ACC	ATC	CAC	TAC	AAC	TAC	ATG	TGT	AAC	AGT	720
	Val	Gly	Ser	Asp	Cys	Thr	Thr	Ile	His	Tyr	Asn	Tyr	Met	Cys	Asn	Ser	
					720					725					730		
40	TCC	TGC	ATG	GGC	GGC	ATG	AAC	CGG	AGG	CCC	ATC	CTC	ACC	ATC	ATC	ACA	768
	Ser	Cys	Met	Gly	Gly	Met	Asn	Arg	Arg	Pro	Ile	Leu	Thr	Ile	Ile	Thr	
			735					740						745			
45	CTG	GAA	GAC	TCC	AGT	GGT	AAT	CTA	CTG	GGA	CGG	AAC	AGC	TTT	GAG	GTG	816
	Leu	Glu	Asp	Ser	Ser	Gly	Asn	Leu	Leu	Gly	Arg	Asn	Ser	Phe	Glu	Val	
			750					755					760				
50	CGT	GTT	TGT	GCC	TGT	CCT	GGG	AGA	GAC	CGG	CGC	ACA	GAG	GAA	GAG	AAT	864
	Arg	Val	Cys	Ala	Cys	Pro	Gly	Arg	Asp	Arg	Arg	Thr	Glu	Glu	Glu	Asn	
		765					770					775					
55	CTC	CGC	AAG	AAA	GGG	GAG	CCT	CAC	CAC	GAG	CTG	CCC	CCA	GGG	AGC	ACT	912
	Leu	Arg	Lys	Lys	Gly	Glu	Pro	His	His	Glu	Leu	Pro	Pro	Gly	Ser	Thr	
						785					790					795	
60	AAG	CGA	GCA	CTG	CCC	AAC	AAC	ACC	AGC	TCC	TCT	CCC	CAG	CCA	AAG	AAG	960
	Lys	Arg	Ala	Leu	Pro	Asn	Asn	Thr	Ser	Ser	Ser	Pro	Gln	Pro	Lys	Lys	
					800					805					810		
65	AAA	CCA	CTG	GAT	GGA	GAA	TAT	TTC	ACC	CTT	CAG	ATC	CGT	GGG	CGT	GAG	1008
	Lys	Pro	Leu	Asp	Gly	Glu	Tyr	Phe	Thr	Leu	Gln	Ile	Arg	Gly	Arg	Glu	
				815					820					825			
70	CGC	TTC	GAG	ATG	TTC	CGA	GAG	CTG	AAT	GAG	GCC	TTG	GAA	CTC	AAG	GAT	1056

Arg Phe Glu Met Phe Arg Glu Leu Asn Glu Ala Leu Glu Leu Lys Asp
830 835 840

5 GCC CAG GCT GGG AAG GAG CCA GGG GGG AGC AGG GCT CAC TCC AGC CAC 1104
Ala Gln Ala Gly Lys Glu Pro Gly Gly Ser Arg Ala His Ser Ser His
845 850 855

10 CTG AAG TCC AAA AAG GGT CAG TCT ACC TCC CGC CAT AAA AAA CTC ATG 1152
Leu Lys Ser Lys Lys Gly Gln Ser Thr Ser Arg His Lys Lys Leu Met
860 865 870 875

TTC AAG ACA GAA GGG CCT GAC TCA GAC TGA 1182
Phe Lys Thr Glu Gly Pro Asp Ser Asp
880

15

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:
20 (A) LENGTH: 393 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Met Glu Glu Pro Gln Ser Asp Pro Ser Val Glu Pro Pro Leu Ser Gln
1 5 10 15

30 Glu Thr Phe Ser Asp Leu Trp Lys Leu Leu Pro Glu Asn Asn Val Leu
20 25 30

35 Ser Pro Leu Pro Ser Gln Ala Met Asp Asp Leu Met Leu Ser Pro Asp
35 40 45

Asp Ile Glu Gln Trp Phe Thr Glu Asp Pro Gly Pro Asp Glu Ala Pro
50 55 60

40 Arg Met Pro Glu Ala Ala Pro Pro Val Ala Pro Ala Pro Ala Ala Pro
65 70 75 80

Thr Pro Ala Ala Pro Ala Pro Ala Pro Ser Trp Pro Leu Ser Ser Ser
85 90 95

45 Val Pro Ser Gln Lys Thr Tyr Gln Gly Ser Tyr Gly Phe Arg Leu Gly
100 105 110

Phe Leu His Ser Gly Thr Ala Lys Ser Val Thr Cys Thr Tyr Ser Pro
50 115 120 125

Ala Leu Asn Lys Met Phe Cys Gln Leu Ala Lys Thr Cys Pro Val Gln
130 135 140

55 Leu Trp Val Asp Ser Thr Pro Pro Pro Gly Thr Arg Val Arg Ala Met
145 150 155 160

Ala Ile Tyr Lys Gln Ser Gln His Met Thr Glu Val Val Arg Arg Cys

	165	170	175
	Pro His His Glu Arg Cys Ser Asp Ser Asp Gly Leu Ala Pro Pro Gln 180 185 190		
5	His Leu Ile Arg Val Glu Gly Asn Leu Arg Val Glu Tyr Leu Asp Asp 195 200 205		
10	Arg Asn Thr Phe Arg His Ser Val Val Val Pro Tyr Glu Pro Pro Glu 210 215 220		
	Val Gly Ser Asp Cys Thr Thr Ile His Tyr Asn Tyr Met Cys Asn Ser 225 230 235 240		
15	Ser Cys Met Gly Gly Met Asn Arg Arg Pro Ile Leu Thr Ile Ile Thr 245 250 255		
	Leu Glu Asp Ser Ser Gly Asn Leu Leu Gly Arg Asn Ser Phe Glu Val 260 265 270		
20	Arg Val Cys Ala Cys Pro Gly Arg Asp Arg Arg Thr Glu Glu Glu Asn 275 280 285		
25	Leu Arg Lys Lys Gly Glu Pro His His Glu Leu Pro Pro Gly Ser Thr 290 295 300		
	Lys Arg Ala Leu Pro Asn Asn Thr Ser Ser Ser Pro Gln Pro Lys Lys 305 310 315 320		
30	Lys Pro Leu Asp Gly Glu Tyr Phe Thr Leu Gln Ile Arg Gly Arg Glu 325 330 335		
	Arg Phe Glu Met Phe Arg Glu Leu Asn Glu Ala Leu Glu Leu Lys Asp 340 345 350		
35	Ala Gln Ala Gly Lys Glu Pro Gly Gly Ser Arg Ala His Ser Ser His 355 360 365		
40	Leu Lys Ser Lys Lys Gly Gln Ser Thr Ser Arg His Lys Lys Leu Met 370 375 380		
	Phe Lys Thr Glu Gly Pro Asp Ser Asp 385 390		